PATENT--FEE

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:

WILLIAM ERNEST PULLMAN ET AL.

Serial No.: 10/031,556

Filed: October 19, 2001

For: **UNIT DOSAGE FORM**

Attorney Docket No. 29342/36206A

Group Art Unit: 1614

Examiner: Rebecca Cook

I hereby certify that this paper is being deposited with the United States Postal Service with sufficient postage, as first class mail, in an envelope addressed to:
Commissioner for Patents
P.O. Box 1450
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Dated: July 21, 2004

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DECLARATION OF DR. GREGORY D. SIDES, M.D., F.A.C.E.P., F.A.C.P.
UNDER 37 C.F.R. §1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

NOW COMES Dr. Gregory D. Sides, Declarant herein, and states as follows:

1. I presently hold the position of Medical Director, Primary Care Products, Cialis® Product Team at Eli Lilly and Company, Lilly Corporate Center, Indianapolis, Indiana 46285.

2. My previous positions were:

Director, Bioproduct Medical, Eli Lilly and Company, Indianapolis, Indiana (Jan 2002 – Jan 2003)

Director of Operations, Global Clinical Research, Eli Lilly and Company, Indianapolis, Indiana (Feb 2001 – Jan 2002)

Acting Director, Cardiovascular Medical, Eli Lilly and Company, Indianapolis, Indiana (Jul 2000 – Feb 2001)

Senior Clinical Research Physician, Cardiovascular, Medical, Eli Lilly and Company, Indianapolis, Indiana (Jan 1999 - Jul 2000)

Clinical Research Physician, Cardiovascular Division, Eli Lilly and Company, Indianapolis, Indiana (Jul 1994 - Dec 1998)

Clinical Research Physician, Infectious Diseases Division, Eli Lilly and Company, Indianapolis, Indiana (Mar 1990 - Jul 1994)

Associate Clinical Research Physician, Infectious Diseases Division, Eli Lilly and Company, Indianapolis, Indiana (Feb 1988 – Mar 1990)

Partner, Kirtley, Paschall, Sides Emergency Physicians, Inc., Danville, Indiana (Nov 1984 – Mar 1988)

Hendricks Community Hospital, Danville, Indiana (Nov 1984 – Mar 1988)

Emergency Physician, Midwest Medical Management, Inc. Indianapolis, Indiana (Jul 1983 – Nov 1984)

3. I received a degree in Medicine from the Indiana University of Medicine, Indianapolis, Indiana in 1980. I received a B.S. in Chemistry, Magna Cum Laude, from Indiana State University, Terre Haute, Indiana in 1977.

I completed an Internship and Residency in Internal Medicine at Methodist Hospital, Indianapolis, Indiana (1980-1983).

I am board certified in Internal Medicine and Emergency Medicine: Board of Certification: Diplomate, American Board of Internal Medicine, September 14, 1983 (#092096); Diplomate: American Board of Emergency Medicine, March 17, 1989 – December 31, 1999, Recertification, December 24, 1998 – December 31, 2008 (#870725).

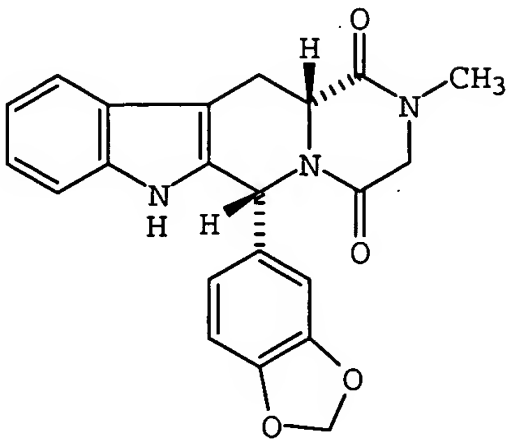
4. I have practiced medicine for twenty three (23) years, conducted research, published about 28 articles, 4 book chapters and 35 abstracts, and presented lectures at numerous conferences, served as a member on numerous editorial boards and scientific or medical advisory boards, and have a membership in numerous societies, such as American Association of Pharmaceutical Physicians, American College of Emergency Physicians, and American College of Physicians.

5. One of my main fields of research and interest is in the field of Internal Medicine, in particular primary care product, cardiovascular, and infectious diseases.

6. I have read and understand U.S. Patent Application Serial No. 10/031,556, and I am familiar with the May 21, 2004 Office Action (Final) in the above-identified application.

7. The invention disclosed in that application is directed to a method of treating sexual dysfunction (Claims 11-17 and 20-23), including, but not limited to, male erectile dysfunction and female sexual arousal disorder, which comprises orally administering to a patient in need thereof one or more unit dose

containing about 1 to about 20 mg of Compound (I) (also refer herein as "tadalafil"), up to a maximum total dose of 20 mg per day.



(I)

8. The present invention is based on detailed experiments and clinical trials, and the unexpected discovery of a unit dosage form incorporating about 1 to about 20 mg of Compound (I) that, when orally administered, effectively treats sexual dysfunction and substantially reduces various undesirable adverse events.

9. The new and surprisingly unexpected results achieved by the present invention are illustrated in Example 7 of the specification in the tables at pages 31 and 32, which show that the lower doses of Compound (I) are not only efficacious but also more tolerable than higher doses (i.e., doses above 20 mg) in treating male erectile dysfunction.

10. Example 7 of the specification in the table at page 31 specifically shows efficacy of Compound (1) at doses ranging from 2 mg to 100 mg evaluated by IIEF. The Table below shows that the efficacy of Compound (I) at 20 mg dose, from an analysis of pooled data from 11 randomized, double-blind, 12-week placebo-controlled trials, is comparable with 50 mg dose (data from Example 7 of the specification).

Table: Efficacy at 20 mg dose and 50 mg dose

	Placebo [1] (N = 638)	**Tadalafil** [1] **20 mg** (N = 1143)	**Placebo** [2] (N = 131)	**Tadalafil** [2] **50 mg** (N = 52)
Efficacy measure	*Change	*Change	*Change	*Change
IIEF EF domain	0.9	8.6	0.8	9.8

[1] Data from an analysis of pooled data from 11 randomized, double-blind, 12-week placebo-controlled trials
[2] Data from the table of Example 7 of the specification (an analysis of data pooled from three Phase 2 studies)
* Change = change from baseline in the erectile function domain of the International Index of Erectile Function (IIEF): Mean

11. The data in paragraph 10 shows that dose at 20 mg is efficacious in treating erectile dysfunction; the mean IIEF EF domain score increased by 8.6 points for 20 mg tadalafil compared to a less then 1 point in the placebo group (0.9). Similarly, the mean IIEF EF domain score increased by 9.8 compared to a less than 1 point in the placebo group (0.8) for 50 mg dose as shown above. Therefore, the efficacy of 20 mg dose is comparable to the efficacy of 50 mg dose.

12. All statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true; further, these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or document or any patent resulting therefrom.

Gregory D. Sides, M.D.

Date: 14 July 2004, 2004